

Орросра
Oct 29, 1952

Dear Joshua,

I am answering your letter of Sept. 18 with more than one month delay. I have been busy at work on one strain, and hoped to get more information out of it before writing you, as this might also involve a change in symbolism. However, the change is quite trivial and you may approve it even if the evidence is not final, or reject it altogether.

You may remember that in our JGM paper a strain is mentioned, which is a BM-F- I isolated early in Cambridge. It has the curious property of crossing with a frequency 25x smaller to F+ than other F- strains. It does not cross to F-. When I tried to infect it with F+ I did not succeed, even in conditions in which an ordinary F- strain, in the same mixture, was infected in 100% of the cases. When crossed to F+, there was a segregation into F+ and F- in the progeny, and, what is funnier, a 1:1 segregation in 3 ~~independent~~ crosses to 3 independent F+ auxotrophs. Analysis of one of these showed no linkage with any of 7 markers. I do not yet know enough of the properties of the ~~progeny~~ progeny, in respect of F+ infectability, segregation ~~rates~~ pattern and F+:F- segregation on recrossing to make a precise statement, but ~~the~~ I have another experiment (still fairly small) showing that this F- strain is a strain resistant to the virus, and which I am therefore provisionally calling F^r. This experiment can be called one testing absorption of F+, although I still have not F+ in cell-free condition. A suspension of F+ cells is incubated with an excess of F- cells for 45', in aeration, then a small amount of F- cells of a distinguishable type are added and incubation continued for 30'. Finally, the two types of F- are separated, and the second added is tested for F+. When, in such an experiment, the first F- added is an ordinary one, all the ~~latter~~ cells ~~are not~~ of the F- added as second are not infected, although they would be infected in controls. The first F- has absorbed all the available virus which is only slowly formed. When, however, F^r cells are used as the first F- addition, and ordinary F- for the second, the latter are infected, as if F^r had not absorbed the virus. Incidentally, Hfr behaves in this experiment as F^r.

I have no good explanation for the low frequency of recombination, except that there is also a change in segregation pattern (chromosome mutation decreasing exchange in TL-M region?). As to the 1:1 segregation, perhaps the easiest explanation is that we have here a locus for maintenance of the virus, and that this locus is on a chromosome not containing loci TL, Lac, Gal, Xyl, Mal, S, B₁, Ara, M. I am now testing new mutants for linkage. If this is true, then we have a situation similar to kappa, sigma, lambda etc. It might then be better to call ϕ the virus

You are quite right about the circular flavor of the argument (3) at page 18. I should propose the following alteration, which perhaps obtains the ~~saméka~~ result as th one you suggest, without too serious ~~alteration~~ :

"Hfr forms an apparent exception to the rule that, in K-12, the presence of F (i.e. of the F⁺ state) in one of the mates is essential for recombination to occur. This rule would mean etc." All the rest unchanged.

Concerning p. 21, I am not satisfied about the hypothesis of the different degree of ploidy. It seems very difficult to test ~~and~~ numerically; a very rough test indicates that it does not work, so that it may be preferable to dispose of it altogether, and remain ~~in~~ the first. Perhaps one way would be to alter the text as follows : "~~There is~~ At least one hypothesis, based on Mendelian theory, can be put forward to account for them: the elimination of a specific segment of the chromosome contributed by the F⁺ parent may take place regularly at every fertilization. There is at present no definite evidence to suggest whether such elimination might occur during formation of the F⁺ gametic cell, during fertilisation, or at the ensuing reduction." The paper might perhaps end thus, and we could delete all the rest. My objection to your interpretation of elimination after fertilisation is that homozygous diploids at one locus may originate through somatic c.o. in an unreduced diploid.

If you approve these corrections I shall incorporate them directly in the proofs when they come.

Finally, I quite agree about your suggestion, of not giving Hfr to other workers for the time being. However, I find myself in some embarrassment on a specific case. Last summer I saw Delbrück at Royaumont, and asked him about results M. Vogt had obtained with Hfr, which I had sent to him from Cambridge two years ago. He said he and she found it quite normal in recombination behaviour, and seemed to doubt the whole story. I therefore promised I would send the strain again. I have not sent it, and think I prefer to wait, in view of what you tell me. We might perhaps agree that I send it later on, at a date convenient for both of us, when the major facts we are interested in at the moment will be known, and reserving perhaps some special use of the strain if necessary. By the way, I have no progress on cytology. Have you ?

One technical point: I find a method of crossing which I call SAT¹ rather useful. It is the usual streptomycin azide reinforced

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by T_1 in coupling with azide in view of the close linkage. $S^r \times$
 $Az^r T_1$ are incubated together overnight in aeration, then plated
 (centrifugation may be useful for enrichment) on $StAzT_1$. The yield
 is about 10^{-7} . Controls ~~fixing~~ are clear, which is the only advan-
 tage in respect of $S Az$ crossings. ~~The yield is about 10^{-7}~~ . I
 find this useful when testing transductions, as it is much more
 expedite than any other method. I have prepared sera against F^+
 and F^- to see if the difference could be detected with antisera
 but have not yet started absorptions.

Yours

Luca.